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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/516,858	07/21/2005	Bengt Herslof	C2432.0060	7315

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EXAMINER	
WALLENHORST, MAUREEN	

ART UNIT	PAPER NUMBER
1743	

DATE MAILED: 05/25/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/516,858	HERSLOF ET AL.	
	Examiner	Art Unit	
	Maureen M. Wallenhorst	1743	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 March 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,15-19,22,24-27 and 29-40* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,15-19,22,24-27 and 29-40* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

1. Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

2. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

4. Claims 1, 31-32 and 34-39 are rejected under 35 U.S.C. 102(b) as being anticipated by Herslof et al (US Patent no. 5,665,379).

Herslof et al teach of a composition comprising a lipid matrix in combination with a bioactive material. The lipid matrix contains at least one polar lipid and at least one non-polar lipid. The polar lipid is preferably a membrane lipid such as phosphatidylcholine, and the non-polar lipid is preferably chosen from the classes of mono-, di- and tri- glycerides or a mixture thereof. See lines 14-34 in column 4 of Herslof et al. The lipid matrix also contains therein a bioactive material such as a drug, a herbicide, a food or a cosmetic ingredient. See lines 35-50 in column 4 of Herslof et al. The composition also can contain water, ethanol or other solvents in

small amounts. See lines 49-52 in column 6 of Herslof et al. In addition, derivatives of lipids such as polyethylene glycol can also be included in the composition. See lines 20-27 in column 6 of Herslof et al. Herslof et al teach that the lipid matrix composition containing a bioactive material can be used as a pharmaceutical composition in the form of oral tablets. See lines 51-59 in column 4 of Herslof et al. The bioactive material can be fragmented heparin known as Fragmin™. See lines 49-54 in column 7 and examples 12-15 of Herslof et al.

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

7. Claims 33 and 40 are rejected under 35 U.S.C. 103(a) as being unpatentable over Herslof et al. For a teaching of Herslof et al, see previous paragraphs in this Office action.

Herslof et al fails to teach what amount of water to include in the lipid matrix composition. However, it would have been obvious to one of ordinary skill in the art at the time of the instant invention to adjust the amount of the water in the lipid matrix composition taught by Herslof et al to the levels recited in instant claims 33 and 40 since concentration is a result

effective parameter that can be experimentally adjusted so as to optimize a particular procedure performed with a composition or a particular use of a composition.

8. Claims 1, 5-19, 22, 24-27 and 29-40 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nyqvist et al (US Patent no. 5,626,869, submitted in the Information Disclosure Statement (IDS) filed on December 3, 2004) in view of Rosenberg et al (WO 01/91729, also submitted in the IDS filed on December 3, 2004, English language equivalent being US 2003/0161884).

Nyqvist et al teach of a pharmaceutical composition containing a lipid system of at least two lipid components, wherein one of the lipid components is polar and the other is non-polar. The pharmaceutically active compound in the composition is heparin or a fragment thereof (i.e. Fragmin™). A water containing solvent is also included in such an amount that discrete lipid particles are present. An alcohol such as ethanol can also be included in the composition. See example 4 in Nyqvist et al. The polar lipid can include phospholipids such as phosphatidylcholine or glycolipids. Non-polar lipids include mono-, di- or triglycerides. The glycerides have a preferred carbon chain length of between 6 and 12 carbon atoms. The composition can be used for oral administration. See the abstract, columns 1-2, lines 1-32 in column 3, lines 15-37 in column 4, lines 8-21 in column 6 and examples 1-7 in Nyqvist et al. Nyqvist et al fail to teach that the pharmaceutical composition can be in a tablet form.

Rosenberg et al teach of a solid composition containing heparin, a lipid component and a polymer. The lipid component constitutes mono-, di- or triglycerides having unsaturated fatty acid esters where the fatty acids have 8-18 carbon atoms. Preferred polymers include polyvinyl pyrrolidone and cellulose derivatives. The composition can be formed as powdered particles,

capsules, pellets, tablets or preferably tablets with an outer coating of excipients. The composition is prepared by melt extrusion at 80-100 degrees Celsius, cooling and then forming a powder, capsule or tablet by grinding, compression, casting, injection molding, tableting under pressure or tableting under pressure with heat. Water or alcohol can be used as a solvent. See the abstract and paragraph nos. 0024, 0026, 0034, 0056-0057, 0067, 0100-0112, and 0122-0126 in Rosenberg et al (US 2003/0161884). Rosenberg et al also teach that the pharmaceutical composition can be used for the oral administration of heparin or a fragment thereof to a patient who has a condition such as thrombosis, pulmonary embolism, myocardial infarction, stroke and cardiovascular disorders. See paragraph nos. 0138 and 0141-0142 of Rosenberg et al.

Based upon the combination of Nyqvist et al and Rosenberg et al, it would have been obvious to one of ordinary skill in the art at the time of the instant invention to formulate the pharmaceutical composition containing a polar lipid, a non-polar lipid and heparin taught by Nyqvist et al into a tablet form using one of the common tablet production procedures disclosed by Rosenberg et al since Rosenberg et al teach that it is known in the art to administer heparin to patients in need thereof in a pharmaceutical tablet form, wherein the tablet contains therein heparin and a lipid component that serves to enhance the biological absorption and solubilization of heparin into a patient's bloodstream. It also would have been obvious to one of ordinary skill in the art to adjust the amounts of the various components in the pharmaceutical composition taught by Nyqvist et al to the amounts as recited in the instant claims since concentration is a result effective parameter that can be experimentally adjusted so as to optimize a particular procedure performed with a composition or a particular use of a composition.

9. Applicant's arguments filed March 16, 2006 have been fully considered but they are not persuasive.

The declaration filed on March 16, 2006 is acceptable, and the previous objection made thereto in the last Office action mailed on November 16, 2005 has been withdrawn. The previous objections to the abstract and claims in the last Office action have also been withdrawn in view of Applicants' amendments thereto. In addition, the previous rejections of the claims under 35 USC 112, first paragraph and under 35 USC 112, second paragraph have been withdrawn in view of Applicants' amendments to the claims.

Applicants argue the rejection of the claims under 35 USC 102(b) as being anticipated by Herslof by stating that Herslof does not disclose a solid composition having a melting point of at least 25^0C since the biosome forming matrix (BFM) taught by Herslof is either a liquid or a semi-solid. In response to this argument, it is noted that Herslof only teaches that the composition is liquid or semi-solid at room temperature, which is about 21-25^0C. See lines 26-27 in column 4 of Herslof. Since the solid composition recited in the instant claims has a melting point of about 25^0C, it melts at about room temperature to form a liquid/semi-solid. Therefore, the composition of the instant invention is also a liquid/semi-solid at room temperature, similar to the composition taught by Herslof. In other words, the compositions are in the same state or phase at room temperature. Since the compositions of the instant invention and as taught by Herslof contain the exact same components (i.e. a polar lipid, a non-polar lipid and a bioactive component like heparin) therein, and since the melting point of a material refers to the point at which a solid material undergoes conversion to a liquid state, one can assume that

the composition taught by Herslof would become a solid at a temperature below room temperature (i.e. below about 25^0C), similar to the composition of the instant invention.

Applicants argue the rejection of the claims under 35 USC 103 as being obvious over Nyqvist in view of Rosenberg by stating that Nyqvist fails to teach a solid composition in the form of a tablet, but rather only teaches a liquid or semi-solid composition similar to Herslof, and that in Rosenberg, a polymer is required in order to render the composition solid. In response to these arguments, it is first noted that the process of melting is a conversion of a material from a solid state to a liquid state. Since the melting point of the composition recited in the instant claims is about 25^0C, it is known that the composition is a solid below 25^0C and a liquid or semi-solid at or above 25^0C. The instant specification states that when forming the heparin composition of the invention, the two types of lipids are mixed with heparin at a temperature above the melting point of the lipids (i.e. above 25^0C), and then cooled to a temperature below the melting point. The cooling causes a solid (i.e. powder) to form. Similarly, in Nyqvist, the same type of lipids as used in the instant invention (i.e. phospholipids, glycerides) are mixed with heparin (i.e. Fragmin™) and stirred at an elevated temperature. See examples 6-7 in Nyqvist. At this elevated temperature, the composition is in a liquid state. However, once the composition is cooled to below the melting temperature of the lipids (i.e. about 25^0C since the same type of lipids are used in Nyqvist as are used in the invention that have a melting point of about 25^0C), they change to the solid phase. When the lipid formulation containing heparin therein is combined with water in Nyqvist, the lipids remain in the solid state since lipids, by definition, are insoluble in water. Therefore, contrary to Applicants' argument, the lipid

formulation containing heparin taught by the primary reference to Nyqvist can be in the solid state depending upon the temperature at which it is held at.

In addition, the secondary reference to Rosenberg does not directly teach that a polymer is necessary to form a solid composition of heparin and a lipid because a lipid at a temperature below its melting point would already be a solid. Rather, Rosenberg teaches that a composition containing heparin and a lipid component can advantageously be converted into a solid tablet form by adding suitable excipients to the composition at a high temperature, and then shaping the composition by extrusion after cooling and solidification. See paragraph no. 0173 in Rosenberg. The primary reference to Nyqvist teaches of administering oral pharmaceutical compositions of heparin to humans, and Rosenberg provides the motivation to convert these oral pharmaceutical compositions into tablets for ease of administration and uniformity of dosage.

For all of the above reasons, Applicants' arguments are not found persuasive.

10. THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maureen M. Wallenhorst whose telephone number is 571-272-1266. The examiner can normally be reached on Monday-Thursday from 6:00 AM to 4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jill Warden, can be reached on 571-272-1267. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Maureen M. Wallenhorst
Primary Examiner
Art Unit 1743

mmw

May 17, 2006

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